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09/760,285	01/15/2001	Nicholas C. Nicolaides	MOR-0017	2664

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EXAMINER	
NGUYEN, DAVE TRONG	

ART UNIT	PAPER NUMBER
1632	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/760,285	Applicant(s) Nicolaides
	Examiner Dave Nguyen	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 15, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 4-82* is/are pending in the application.

4a) Of the above, claim(s) *14-21, 25, 26, 30-67, 69, and 71* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4-13, 22-24, 27-29, 68, 70, and 72-82* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jan 15, 2001* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *16*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 2, 3 have been canceled, claims 72-82 have been added, claims 1, 4-13, 23, 70 have been amended by the amendment filed November 15, 2002.

Applicant's election with traverse of Group VI claims (claims 23, 24, 27-29, 68, 70), species of 1, 2-dimethyl anthracene, wherein R1 and R2 are methyl groups and each of R3-R10 is hydrogen, in the response filed May 28, 2002 is acknowledged. The examiner also acknowledges that DMBA is not the elected species, and this office action has been modified to reflect the acknowledgement. In addition, the examiner has rejoined of the species of 9,10-dimethyl anthracene with the elected species of 1, 2-dimethyl anthracene for the purpose of compact prosecution. Thus, the examiner acknowledged that the elected species are 1, 2-dimethyl anthracene, and 9,10-dimethyl anthracene . As such, the new grounds of rejection are applicable to the elected species. All previous prior art rejections have been withdrawn by the examiner.

Claims 14-21, 25-26, 30-67, 69, 71 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claimed invention.

Elected claims 1, 4-13, 22-24, 27-29, 68, 70, 72-82 readable on the elected invention are pending for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72-82 are rejected under 35 U.S.C. 112, first paragraph, because the specification is only enabling for claims limited to:

A method for generating a genotoxic mutation in mismatch repair gene in a cell of a non-human organism, comprising administering to at lest one cell of said organism an effective amount of anthracene, wherein said anthracene has the formula as recited in claim 72.

The specification is not enabling for claims directed to any other claimed embodiment within the elected claimed invention. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, particularly in view of the same reasons as set forth in the enablement rejection stated in the previous office action.

Applicant's response has been considered and not found persuasive because the phrase "A method for generating a genotoxic mutation in mismatch repair gene in a cell *in vitro* or in a cell of a non-human organism" is not recited in the amended or newly added claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13, 23-24, 27-29, 68, 70 are rejected under 35 USC 102(b) as being anticipated by Traczewska *et al.* (Acta Microbiologica Polonica, Vol. 40, 3, 4, 235-241, 1991).

Traczewska *et al.* teach a method of administering anthracene and 9, 10-dimethylanthracene as a sole carbon sourcefor the growth of bacterial cell isolated from waters. Given the method steps and materials disclosed in the Traczewska *et al.* reference are identical to that of the claims, the method of Traczewska *et al.* would necessarily exhibit the biological function intended for 9, 10-dimethylanthracene.

Claims 1, 4-13, 22-24, 27-29, 68, 70, 72-82 are rejected under 35 USC 102(b) as being anticipated by either LaVoie, Carcinogenesis, Vol. 6, pp. 1483-1488, 1985, or Cerniglia *et al.*, Applied and Environmental Microbiology, Vol. 56, No. 3, pp. 661-668, 1990.

LaVoie teaches a method of administering an suitable or effective amount of numerous methylated anthracenes, *e.g.,* 1-, 2-, 99-, 2,9- and 9,10-demethylanthracene 9, as a carbon source for inducing tumor-initiating activity, mutagenicity, and metabolism of methylated anthracenes in an organism, *S. typhimurium* TA 98 and TA100. LaVoie also reviews the art of employing methylated anthracenes as a mutagene and teaches that on the basis oh his study,

wherein a different dose of methylated anthracenes was employed, the tumor-innitiating activity of methylated anthracenes can be initiated on mouse skin (Tables I and II, page 1485, column 2, p. 1487, column 1 bridging column 2.

Given the method steps and materials disclosed in LaVoie are identical to that of the claims, the method of LaVoie would necessarily exhibit the biological function intended for the employed methylated anthracene.

Cerniglia *et al.* teaches a method of administering 9, 10-dimethylanthracene as a carbon source for the growth of the fungus *Cuuninghamella elegans* ATCC 36112.

Given the method steps and materials disclosed in Cerniglia *et al.* are identical to that of the claims, the method of Cerniglia *et al.* would necessarily exhibit the biological function intended for 9, 10-dimethylanthracene.

Claims 1, 4-13, 22-24, 27-29, 68, 70, 72-82 are rejected under 35 USC 103(a) as being unpatentable over LaVoie, Carcinogenesis, Vol. 6, pp. 1483-1488, 1985.

To the extent that the claims embrace the use of 1,2-dimethylanthracene to induce genetoxic hypermutation or tumor induced activity in any cell *in vitro* or *in vivo,* LaVoie teaches a method of administering an suitable or effective amount of numerous methylated anthracenes, *e.g.,* 1-, 2-, 99-, 2,9- and 9,10-dimethylanthracene 9, as a carbon source for inducing tumor-initiating activity, mutagenicity, and metabolism of methylated anthracenes in an organism, *S. typhimurium* TA 98 and TA100. LaVoie also reviews the art of employing methylated anthracenes as a mutagene and teaches that on the basis of his study, wherein a different dose of methylated anthracenes was employed, the tumor-innitiating activity of methylated anthracenes can be initiated on mouse skin (Tables I and II, page 1485, column 2, p. 1487, column 1 bridging column 2.

Given the method steps and materials disclosed in LaVoie are identical to that of the claims, the method of LaVoie, which teaches methylated anthracenes is a mutagen, would

necessarily exhibit the biological function intended for the employed methylated anthracene. LaVoie does not teach explicitly that 1,2-dimethylanthracene induces genetoxic hypermutation or tumor induced activity in any cell *in vitro* or *in vivo.*

As such, it would have been obvious for one of ordinary skill in the art to have employed 1,2-dimethylanthracene as a matter of obvious design choice to induce genetoxic hypermutation or tumor induced activity in any cell *in vitro* or *in vivo.* One of ordinary skill in the art of carcinogenesis would have been motivated to employ any methylated anthracene to study its effect in inducing genetoxic hypermutation or tumor induced activity in any cell *in vitro* or *in vivo* because of the entire teaching of LaVoie which teaches in his method, an effective amount of numerous methylated anthracenes, *e.g.,* 1-, 2-, 99-, 2,9- and 9,10-dimethylanthracene 9, do generate tumor-initiating activity, mutagenicity, and metabolism of methylated anthracenes in organism, *S. typhimurium* TA 98 and TA100 and mouse. One would have expected that 1,2-dimethylanthracene would have necessarily produce at least the same effect as demonstrated for other closely related methylated anthracenes employed in LaVoie, particularly since LaVoie teaches that on the basis of his study, wherein a different dose of methylated anthracenes was employed, the tumor-innitiating activity of methylated anthracenes can be initiated on mouse skin and in *S. typhimurium.* Moreover, the tumor-initiating activity, mutagenicity, and metabolism of methylated anthracenes as shown in LaVoie would necessarily generates a hypermutable cell wherein the presence of methylated anthracenes would necessarily inhibit activities of a mismatch repair in the cell, particularly since LaVoie employs identical method steps and materials as embraced by the claims, and particularly since the as-filed specification teaches that any methylated anthracene as embraced and cited in the claims would exhibit the inhibitory activity against a mismatch repair gene in the cell.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 1, 4-13, 22-24, 27-29, 68, 70, 72-82 are rejected under 35 USC 103(a) as being unpatentable over any of LaVoie, Carcinogenesis, Vol. 6, pp. 1483-1488, 1985, Chakravarti *et al.* (PNAS, Vol. 92, pp. 10422-10426, 1995) or Zhang (US 20002/0064879 A1), taken with Hoorn and Myers *et al.,* Biochemical and Biopysical Res. Communications, Vol. 151, No. 3, pp. 1441-1445, 1988.

To the extent that the claims embrace the use of 1,2-dimethylanthracene to induce genetoxic hypermutation or tumor induced activity in any cell *in vitro* or *in vivo,* LaVoie teaches a method of administering an suitable or effective amount of numerous methylated anthracenes, *e.g.,* 1-, 2-, 99-, 2,9- and 9,10-demethylanthracene 9, as a carbon source for inducing tumor-initiating activity, mutagenicity, and metabolism of methylated anthracenes in an organism, *S. typhimurium* TA 98 and TA100. LaVoie also reviews the art of employing methylated anthracenes as a mutagene and teaches that on the basis oh his study, wherein a different dose of methylated anthracenes was employed, the tumor-innitiating activity of methylated anthracenes can be initiated on mouse skin (Tables I and II, page 1485, column 2, p. 1487, column 1 bridging column 2.

Given the method steps and materials disclosed in LaVoie are identical to that of the claims, the method of LaVoie, which teaches methylated anthracenes is a mutagen, would necessarily exhibit the biological function intended for the employed methylated anthracene. LaVoie does not teach explicitly that 1,2-dimethylanthracene induces genetoxic hypermutation or tumor induced activity in any cell *in vitro* or *in vivo.*

Chakravarti *et al.* teaches a method of inducing a genetoxic hypermutaiton of *ras* oncogenes in mice by exposing the skin cells of mice to carcinogene-DNA adducts and/or mutagens, *e.g.,* DMBA (abstract, page 10422, and page 10423). A DNA binding assay was also disclosed in Chakravarti *et al.* to determine the presence the mutant gene sequence.

Zhang teaches a method for obtaining a plant with a genetic lesion in a gene sequence flanked in a wild type chromosome by known polynucleotide sequences, comprising exposing the plant and cells thereof to a mutagenic chemical substance. Chakravarti *et al.* and Zhang do not

teach that the chemical substance is 9, 10-dimethylanthracene. A DNA binding assay was also disclosed in Zhang to determine the presence the mutant gene sequence.

However, at the time the invention was made, Hoorn teaches that anthracene is a potent chemical mutagen for inducing random mutation in gene sequences.

Myers *et al.* teaches a method of administering anthracene as a carbon source for monitoring its bioalkylation and biooxidation of the carbon source *in vitro* and *in vivo,* and that anthracene when converted into 9, 10-dimethylanthracene would possess both meso-anthracenic reactive centers and carcinorgenic activity.

Thus, it would have been obvious for one of ordinary skill in the art to employ 9, 10-dimethylanthracene as the mutagen in either the method of Chakravarti *et al.* or Zhang. One would have been motivated to do so because Hoom teaches that anthracene is a potent chemical mutagen for inducing random mutation in gene sequences, because Myers *et al.* teaches that 9, 10-dimethylanthracene is the main reactive group for causing mutagenesis or carcionogenesis in cells.

To the extent that the claims are readable on the step of removing the carcinogens and/or mutagens from the medium prior to the analysis step, the claims are also obvious over the cited prior art because one of ordinary skill in the art would have been motivated to do the same in order to monitor the exposing time of carcinogens to the cells.

Thus, the claimed invention was as a whole *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER